REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the rejection of the claims.

Claims 49-50, 58-60, and 65 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue these claims in one or more continuation applications. Applicants have also cancelled subject matter relating to inflammation from the claims and reserve the right to pursue this subject matter in a continuation application.

Claims 19, 38, 42, 45, 48, 54, 61 and 72 have been amended to further clarify the claimed invention. Claims 42, 45, 48, 54 and 72 have been amended to correct typographical errors and for claim language consistency. Applicants submit the amendment does not introduce any new matter.

Interview Summary

Applicants thank Examiner Deberry and her supervisor for the interview conducted on August 23, 2007. We discussed the language of claims 19 and 38 with regard to the steps of the method. We also discussed separating claims directed to cancer and those directed to inflammation. We discussed enablement issues.

Claim Objections

Claims 19, 38, and 59 were objected to as not limited to the elected invention. The Final Office Action did not provide any rationale for the rejection. Applicants submit the claims as amended are directed to the elected invention. If the Examiner believes the claims as amended are not limited to the elected invention, Applicants respectfully request that the Examiner provide a basis for the objection.

Enablement

Claims 19, 38, and 42-75 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Office Action alleges claim 38 lacks enablement because specification does not disclose that the claimed method can be used to determine the presence of or predisposition to all types of cancers. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 38 has been amended to recite detecting cancer in only certain types of tissue. The amendment is supported by working Examples 3 and 4. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Office Action also alleges the tumor marker data provided in the specification does not enable the full scope of the claims. The Examiner alleges it is unclear if the nucleic acid levels are enhanced or decreased compared to normal control tissues because of inconsistent expression of the nucleic acid molecules in the same tissues and concludes it is not clear which samples are statistically significant. Applicants respectfully do not agree.

Applicants submit that the Examiner is requiring Applicants to establish enablement to a higher degree of certainty than is required. An enabling disclosure only requires a reasonable correlation to the scope of the claims. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied (*In re Fischer*, 427 F.2d 833, 839 (CCPA 1970)). For a claimed genus, representative examples coupled with a statement applicable to the genus as a whole are ordinarily sufficient to comply with the enablement requirement (MPEP § 2164.02).

The claims have been amended to recite detecting an alteration in expression of the nucleic acid molecules in a tumor cell compared to a normal cell. Table 8 shows expression of the nucleic acid molecules is altered in pancreas, liver, colon, stomach, thyroid, kidney, and bladder cancer cells relative to normal cells from the respective tissues. Table 9 shows expression of the nucleic acid molecules in tumor tissue compared to normal adjacent tissue in the same patient or normal tissue from a different patient. In some instances, expression of the nucleic acid molecules is increased relative to the control (see, for example, colon and liver in Tables 8 and 9). In some instances, expression of the nucleic acid molecules is decreased relative to the control (see, for example, kidney and prostate). Nevertheless, an increase or

decrease in expression of the nucleic acid molecules in tumor cells or tumor tissue relative to the control cells or control tissue was indicative of cancer.

Applicants submit the data provide in Tables 8 and 9 provide a reasonable correlation between an alteration in expression of the nucleic acid molecules in the recited cells and tissues and cancer. Contrary to the Examiner's assertion, Tables 8 and 9 provide a control cell or control tissue for each cell type or tissue type.

Moreover, post filing date information, indicates that the polypeptide comprising SEQ ID NO:6 has been categorized as S100 protein A14. (alignment attached) Members of the S100 family have been implicated as markers for cancer tissue. With respect to the results presented in the application for breast, prostate, and colon cancer, analysis of circulating tumor cells indicates that S100A14 serves as a marker for breast cancer and colon cancer cells. (Smirnov et al,Cancer Res.65:4993(2006))

Citing Barker et al. and Anderson et al., the Examiner alleges that *in vitro* results acquired from tumor cell lines may not correlate with the results obtained from tumor tissue from patients because the cell culturing process alters gene expression and selects subgroups of cells such that the cultured tumor cells are no longer representative of the diseased tissue. Applicants respectfully do not agree.

If the particular model is recognized in the art as correlating to a specific condition, then the model should be accepted as correlating unless the Examiner has evidence that the model does not correlate. *In re Brana*, 34 USPQ2d, 1436, 1441 (Fed. Cir. 1995); MPEP § 2164.02. A rigorous or an invariable exact correlation is not required. *Cross v. Iizuka,* 244 USPQ, 739, 747 (Fed. Cir. 1985).

Applicants submit that the references cited in the Office Action do not provide sufficient evidence that **all** tumor cell lines are not representative of the tumor cells in vivo. Barker et al. contemplates ovarian tumor cells and only discloses that passage of ovarian tumor cell lines **occasionally** results in lack of experimental reproducibility. Anderson et al. identified changes in immunological phenotype of glioblastoma cells cultured in vitro but the functional significance of the changes was not known. In contrast, Applicants studied the expression of the nucleic acid molecules in several tumor cell lines and tumor tissue from patients. In contrast to Anderson et al., Applicants disclose expression of the nucleic acid molecules in the tumor cell

lines (Table 8) correlated with expression of the nucleic acid molecules in tumor tissue (Table 9). For example, expression of the nucleic acid molecules was increased in both liver tumor cells and liver tumor tissue relative to their respective control liver cells and control liver tissue.

Applicants therefore submit the Office Action does not establish that all tumor cell lines are not representative of the tumor cells in vivo. Moreover, none of the particular cell types recited in the claims is disclosed in Barker et al. or Anderson et al.

The Office Action alleges claim 59 is not enabled by the specification because the specification does not teach functional characteristics or mechanisms of action of FCTRX. Applicants respectfully do not agree. While not acquiescing to the rejection and solely to expedite prosecution, Applicants have cancelled claim 59.

The Office Action alleges the specification does not enable methods for determining the presence of inflammation. The Examiner alleges TNF-alpha is a multifunctional cytokine that exerts a myriad of diverse biological functions and that TNF alpha induced expression of the nucleic acids is not tantamount to indicating the presence of inflammation. Applicants respectfully do not agree. While not acquiescing to the rejection and solely to expedite prosecution, applicants have cancelled that subject matter from the current claims. Applicants reserve the right to pursue this subject matter in a continuation application.

The Office Action alleges the specification fails to provide guidance as to what level of expression of a nucleic acid encoding SEQ ID NO:3 or SEQ ID NO:6 would be indicative of a predisposition to cancer or inflammation. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 38 as amended is directed to detecting cancer. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Office Action alleges a nucleic acid molecule encoding a polypeptide having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:6 is not enabled by the specification. Applicants respectfully do not agree. While not acquiescing to the rejection and solely to expedite prosecution, Applicants' claims now refer to a nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

In view of the forgoing, Applicants submit the claims as amended are fully enabled by the specification. Withdrawal of the enablement rejection is respectfully requested.

Written Description

Claims 19, 38, and 42-75 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP § 2163(I) (emphasis added). An Applicant may show possession of an invention by disclosure of sufficiently detailed, relevant identifying characteristics (i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between structure and function, or some combination of such characteristics) that provide evidence that Applicant was in possession of the claimed invention. *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964 (Fed. Cir. 2002); MPEP § 2163(II)(3)(A)(a). An actual reduction to practice, however, is not required for written description. *Falkner v. Inglis*, No. 05-1324, slip. op. at 13 (Fed. Cir. May 26, 2006).

The written description requirement must be applied in the context of the particular invention and state of the knowledge. *Capon v. Eschar*, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005). It is unnecessary to spell out every detail of the invention in the specification. Only enough must be included to convince a person of skill in the art that the inventor possessed the invention. *Falkner v. Inglis*, No. 05-1234, slip. op. at 14 (Fed Cir. May 26, 2006) (citing *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 Fed. Cir. 2005).

Applying these standards, Applicants submit the specification sufficiently describes the claimed genus of polypeptides for the reasons discussed in the Response filed on November 13, 2006. While not acquiescing to the rejection and solely to expedite prosecution, Applicants' claims now refer to a nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

Indefiniteness

Claims 19 and 42-50 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants submit claim 19 as amended fully complies with § 112, second paragraph. Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicants submit the claims are in condition for allowance and respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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